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The University of Toronto Medical Journal

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EDITORIAL.

Vol. IV. has driven the Journal one notch deeper into the life of this university. Members of the staff, recent graduates, and students are increasingly conscious of its existence. We are confident that its disappearance would leave a distinct want.

It is particularly encouraging to find that our subscribers frequently approach one of the Journal staff with suggestions or material.

The Editorial Staff wishes to express its appreciation to those who by giving their time and thought have made these issues possible. We also wish to thank our advisers in the Faculty of Medicine for their encouragement, co-operation and advice. In particular we would like to mention Dr. E. S. Ryerson and Dr. R. I. Harris, who have given much sound advice.

EDITOR 1927-28.

Mr. J. A. Carswell, B.A., has accepted the appointment of Editor-in-Chief of this Journal for the coming session. Under his able direction the Journal is sure to flourish and develope into a still more useful and representative organ. We wish him and his associates every success.

Mr. Burton Yuill has been re-appointed Business Manager of this journal. To his capable management we owe our present sound financial state.

HERE'S A WISE CRACK.

A specialist is one who is learning more and more about less and less.

Dr. R. F. Farquharson is leaving Toronto to spend a year in the Research Unit of the Massachusetts General Hospital. His cheerful willingness to help at all times will be missed by everyone.

Professor J. M. D. Olmstead has been appointed Professor and head of the Department of Physiology in the University of California. Congratulations and best wishes.

SONNET TO A FOREIGN BUTCHER SHOP.*

By N.A.B.

I loathe all horror, but it fascinates,
And so a daily carnage foul I see,
Scarce daring first to let it noticed be,
Though now my eye its very reek elates:
Wide, winy livers spread on bloody plates
And slimy viscous entrail strung in glee
By unclean, pudgy hands for all to see,
The while for garlic garnishing it waits.

And best of all, a fleshless bovine head
With horns chipped off and staring, jellied eyes,
Lies upside down, all slopping, flowing red,
Still goggling at the buying bellied wives,
And ready to serve this retching, crimson feast,
Jabbering, the genial, gory-aproned priest.

* Reprinted from the University College Magazine. Vol. I. No. I. March, 1927.

To T.B.*

Slender, yet strongly pugnacious bacillus,
What though your size is but 3 or 4 μ,
Yet you attack and courageously kill us—
Us, many millions times bigger than you.

Still I do feel some remorse to have slain you
By methods that must have been painful to you,
Feel it unsportsmanlike still when I stain you
With hot Carbol Fuchsin and Methylene Blue.

Valour and virulence, perfectly blending,
Should in some noble achievement have died
Rather than meet an unglorious ending
Mounted and stained on a microscope slide.

You must have had many strenuous tussels—
Lived in a state of perpetual strife,
Struggling with fierce phagocytic corpuscles,
Barely escaping perhaps with your life.

Grappled with murderous opsonins, striving
Cruelly to catch you and cook you entire;
Death in a thousand fierce conflicts surviving,
Only at length on a film to expire.

Had you but died in the lung you invaded,
Fighting, outnumbered by leucocyte foes,
Battling with giant-cells, lonely, unaided—
This would have been a more glorious close.

Then had the foes you so stoutly resisted
Buried you there with the honors of war;
Lying in tough fibrous tissue encysted,
Still might your corse fill young blood-cells with awe.

Yet in your downfall to tears you provoke us;
Even your carcase, in death lying prone,
(Wait half a tick while I get it in focus—
There!) has a delicate grace of its own!

What though no flaunting flagella adorn you,
What though for speed you were never designed,
Let not the motile bacteria scorn you,
Yours is a beauty more staid and refined.

Slender, yet strongly pugnacious bacillus,
As to your beauty we may disagree,
But as to your power to maim and to kill us—
Well—no one would challenge a fight with T.B.

—R.B.P..

* Reprinted from Round the Fountain and St. Bart's Med. Journal. January, 1908.

NOTICE 2T8

PUBLIC HEALTH COURSE

There will be no June number of this Journal. We would recommend the Ladies' Home Journal as a substitute during your course.

Modern Aspects of Cancer Research.

WILLIAM B. BREBNER, M.B.
Fellow of the Chair of Medical Research.

IN surveying the field of Cancer research one is struck with the aptness of Walter Whiteman's remark as quoted in a recent publication: (1) "Dead poets, philosophers, priests, martyrs, artists, inventors, governments long since; language shapers on other shores,—I dare not proceed till I respectfully credit what you have wafted hither. I have perused it, own it is admirable, moving awhile among it; think nothing can ever be greater, nothing can ever deserve more than it deserves. Regarding it all intently and for a long while, then," continues Whitman, "then dismissing it, I stand in my own place with my own day here." Unfortunately there are as yet no Whitemans in the field of cancer research who are able to stand in their own place holding more than a fraction of the total, requisite for the fulfilment of the demand for a solution of the cancer problem.

Malignant disease has been recognized clinically from the time of the Egyptians in 1900, B.C., and since that time glimpses have been caught of the varying conceptions of the disease from surviving records. Cancer research was probably unthought of until cellular pathology became possible with the discovery and use of the microscope. Then Schleiden, Schwann, Remak and Virchow began studies to determine the function of the cells. Typical of the period, and particularly of the scientific world of the time, opinions were positive and vigorously assailed and defended. The importance of cell division and the mechanics of it were of tremendous interest and the facts of the pathology of malignant tissue gradually were established. Though various theories as to the origin of malignant growth have had their period of popularity, but two survive. The first is that of chronic cell irritation. The second that of cell displacement (Vide Cohnheim).

Attempts to Induce Malignant Change in Tissue.

Since 1808 attempts have been made to induce the growth of malignant cells by the displacement, i.e., the transplantation of adult normal, malignant and embryonic tissue, with or without the addition of various other substances. Transplantation is still a favorite method in cancer research and perhaps an observation might be made at this juncture. Any transplantation owes its success to the relationship of the donor to the host (specie and blood group) the vitality of the transplant and the vigor of the host's normal reparative process. This last factor is exceedingly important since it is only reasonable that the sooner the host can furnish capillaries and fibroblasts to sustain the graft the more certain are the chances of survival. Young animals are therefore usually good hosts, a circumstance hardly compatible with the age of appearance of spontaneous tumors. Various irritants have been utilized to produce tumour all without avail until in 1914 Yamagiwce and Itchikawa reported the occurrence of tumors following repeated painting with tar. Their success recalls the failure of Hanau in 1889 to produce tumors by similar treatment. A story which will doubtless be often repeated. Many individual experiments are extremely interesting historically and a large number of these are still stimulating in their suggestion. One large series of experiments by numerous observers deals with the effect of various facts and fat solvents. These are interesting in their association with the modern work of Burrows and Jorstad and the fat soluble Vitamin A of which mention will be made later.

The Transmissibility of Cancer.

The transmissibility of cancer has been of interest for many years and it is recorded

that in 1808 Alibert in Paris injected himself and several students with material taken from a breast carcinoma. This, like many following experiments, was negative in result though there appear to be a number of authentic cases of infection of the attendants and intimates of cases having ulcerated tumors. There are certainly cases which show infection or grafting at sites other than the primary. As for example, carcinoma of the lower lip causing the appearance of a growth on the adjacent area on the other lip or the occurrence of squamous-celled carcinoma of the stomach with the primary on the face, mouth or oesophagus. A few inoperable cases were experimented with and occasionally a tumor was successfully transplanted to another site in the host. Now of course such a possibility is well recognized by our surgeons who practise wide excision and so prevent dissemination of malignant cells throughout the incision. Not long ago a case of a young surgeon was reported who, assisting at an operation for malignant disease, had the scalpel used in excising the tumor dropped on his hand. The blade penetrated the palmar surface and at a later period a tumor appeared at the site of injury, apparently a transplant.

Since the publication of a paper by Jensen in 1903 a new era really started in cancer research. Jensen's paper dealt chiefly with a transmissible tumor of the rat and caught the interest of the experimental pathologists who began to realize the significance of the studies. Loeb and Borrel published comparable studies almost synchronously with Jensen. Yet Jensen's work was not the first in this field, since Hanau in 1889, Pleiffer in 1890, Von Eiselsberg, Moran, Firket and Velice had previously reported transmissible tumors in various animals. Since these early observations a large number of transmissible tumors have been discovered and studied. Much of the systematic work of cataloging the tumors and their variations has been done by the Imperial Research Foundation. Since Hanau's experiments, results have had a new significance because specie cell specificity excludes all the old attempts to transmit cancer to animals of different race than the host.

To trace the various steps would be laborious in such a general review. Rather would I turn to a brief discussion of the more important lines of investigation.

Work of Dr. Maude Slye. (3, 4, 5).

Perhaps no modern research has any greater significance than that of Dr. Maude Slye of Chicago. To prove that cancer is inheritable in mice and that the susceptibility behaves as a Mendelian recessive character as Dr. Slye has done is a scientific fact of prime importance. One cannot but be filled with admiration for an individual who has devoted 17-18 years to a research conducted in a most meticuluous fashion. Dr. Slye is a paragon of conservatism of statement unlike many of her brethren, and nothing of surmise or conjecture is ever published to cause barometric rises of interest and enthusiasm. During her years of work, Dr. Slye has undergone many of the difficulties of the research worker as are sometimes rather picturesquely imagined in the novelist's brain and anyone would be interested to hear of her early trials when research was not fostered, as it is now, by the various foundations.

In studying the cancer tendency, Dr. Slye realized at an early date that her results would be of far greater value if her animals lived out their normal expectancy of life and to that end a most extraordinary system of management has been evolved whereby the mice are ingeniously protected from vermin, epidemic, food contaminations and in fact all the ills that the flesh is heir to. Dr. Slye can now give the family history for many generations of a large number of individual mice and can manipulate her stocks to cause tumor to appear or remain recessive almost at will.

Not only does the cancer tendency appear to be a Mendelian-recessive character, but the site of the tumor follows the same rule. Hence she has races of mice that show mammary carcinoma and only that, and others showing carcinoma of the liver. It is worth while mentioning the fact that a great many common diseases, as nephritis and longevity as well appear to have an hereditary basis from her experiments.

Concluding this portion of the discussion I will quote an example which reveals the second important fact Dr. Slye's work has

brought out. A strain of mice definitely bred for carcinoma of the face will not show the development of tumor growth until the tissues are traumatized in some way. The development of a tumor at the site of injury is the normal response of that particular tissue to damage. The regenerative response is abnormal, leading not to scar formation, but to tumor. Wounds to parts other than the face heal by first intention. The disease would appear from these and other experiments to be a local tissue defect. The regeneration of the local tissue lacks a differentiating mechanism.

Bacterial Organism—Suggested as a Cause. (6).

That cancer may have a bacterial origin has been suggested by several workers, namely Young of Edinburgh, Blumenthal of Berlin, Spengler of Vienna, Nuzum from the United States and Glover of Toronto. These workers have described an organism which apparently has a complex life circle. Glover is of the opinion each worker is dealing with the same organism. Their results are extremely interesting and warrant further examination. Glover has developed an antiserum which has in certain cases caused the disappearance of the carcinoma. He and his associates are of the opinion that serum treatment is most effective following surgery, planned to remove the bulk of the tumor tissue. The treatment is not infallible nor does it cure advanced cases, though symptomatic improvement may follow.

One difficulty with culturing any tissue is that on prolonged incubation bacterial growth may occur in a large number of cases. The organisms from such do not cause tumors nor do they appear to be the organism described by Glover et al. Another difficulty is that many tumors are contaminated while still in the host and on culture show early bacterial growth. Woglom of the Crocker Research Foundation believes that at least 40 per cent. are so infected. Gye mentions the fact too, that contamination is common.

The group of individuals mentioned above are not the only ones who hold that bacteria are responsible for the malignant change. For various reasons their work has been discredited. In the journals one can find papers discussing the possibility of there being a responsible organism. Ewing of New York has remarked that whatever the cause of cancer may be, certainly bacteria are the last possibility.

Tissue Culture. (7, 8).

The technique of growing tissue cells in vitro has improved to such a degree since the pioneer work of Harrison in 1907, that the method is one of considerable importance. Much of the progress has been due to Carrel, Burrows and Lewis. At the present time several different types of cells can be grown in pure culture and strains can be carried with facility for any length of time.

There are, briefly, four main points relative to tissue culture technique.

1. Most types of cells require a skeletal framework on which to grow. The best is the fibrin threads in clotted plasma.

2. Any growing tissues produce toxic metabolites and these cannot be allowed to accumulate. Therefore the culture must be washed, or divided every 24 hours and a portion embedded in fresh plasma, if growth is to continue.

3. Pure plasma is not a readily available source of food, and to insure growth it is necessary to add some growth catalyst or simple food stuff to each culture. This growth-stimulating substance is found most plentifully in an extract of a nine-day embryonic chick. It is also found in an extract of tumor tissue and to a lesser extent in other tissues.

4. Absolute sterility is essential.

On studying malignant cells in culture few differences can be distinguished from normal cells. And no observer has detected any biological differences which have not also been observed in normal cells. There are certain characteristics to be mentioned: Malignant cells, particularly sarcoma cells, unlike all normal cells other than leucocytes, are able to grow and proliferate in a medium containing nothing more than pure plasma. No growth-stimulating substance is necessary. Moreover, sarcoma cells have a remarkable solvent effect on their plasma medium. A third fact is important and may explain some of the propagative and destructive qualities of tumor cells. In a culture of sarcomatous tissue when the cells

are scattered by migration and even when individual cells have no protoplasmic connection with their fellows,—cell division may occur. No other comparable tissue can reproduce itself except it be in protoplasmic contact with other cells.

Tissue cultures are providing an excellent method for examining the mechanisms of immunity and Lumsden of the Lister Institute is working in this field. His papers are well worth reading if one is interested. (11, 12, 13).

Work of Gye. (9).

In 1911 Rous of Rockefeller Institute (14) reported the occurrence of a transmissible tumor of the chicken. Following that date a number of publications described the various characteristics of the tumor. The tumor is remarkably malignant and is transmissible by a cell-free filtrate. Using this tumor, Gye in 1925 reported a series of experiments which have attracted a great deal of attention. He postulated the presence of two factors in an infective, but cell-free extract of the Rous tumor. One he believed to be an ultramicroscopic virus. The other a chemical adjunct which he calls "specific factor." Neither alone will cause a tumor, but in combination the mixture is infective. Gye had several methods for separating the two factors:

1. The specific factor or chemical substance would appear to be thermolabile and the virus not so. The virus is susceptible to chloroform, acriflavine and other germicides. Therefore if two portions of a cell-free extract of the Rous tumor are taken, "A" and "B." "A" is treated with heat (55 degrees for 15 minutes); "B" is treated with chloroform (in definite proportion for a definite time), then neither part is infective alone, but "A" plus "B" will cause a tumor.

2. Gye shows that every tumor contains specific factor and virus. Virus can only be recovered from tumors, other than Rous by incubating the tissue in a special Hartley's broth. The broth from a tumor after 3 to 5 days' incubation is non-infective alone. Specific factor is most plentiful in Rous tumor and obtained from that source and added to the virus from rat tumor will cause Rous sarcoma in fowl.

His experiments appear very convincing. unfortunately no other workers (16, 17) have been able to duplicate his results in any consistent fashion. His work perhaps holds its chief value in the stimulus it gave cancer research.

The Embryonic Cell a Potentially Malignant Cell?

There are now a series of reported experiments which would seem to indicate that the embryonic cell is more or less readily convertible into a malignant one. Carrel has shown that if minced embryonic chick plus a minute quantity of arsenious acid or indol is injected into fowl a typical sarcoma will result, or if a chicken is previously treated with an ethereal solution of tar a tumor will arise from injected embryonic tissue. Bisceglie (15) has reported the development of a sarcoma of the fowl following the injection of embryonic pulp plus an extract of mouse tumor. The above facts would seem to indicate that a "conditioned cell" may become malignant under additional stimulants.

The Work of Burrows and Jorstad. (10).

The above workers have done a stimulating piece of work on the influence of vitamin "A" and "B" on cell growth. They believe that when a portion of tissue is normally functioning a balance exists between vitamin "A" and "B." If for any reason vitamin "A" is removed or vitamin "B" increased in amount, then cancer will result. They explain the incidence of cancer following X-rays, radium, animal parasites and bacteria by saying that the vitamin "B" or growth-stimulating factor is supplied in excess and the circulation to the area is so impeded that vitamin "A" or the growth-controlling factor cannot reach the cells. Coal tar changes the surface tension of the cells, causes crowding and stagnation so that the cells produce and retain an excess quantity of vitamin "B."

In as much as the vitamins are recognized only by their value in feeding experiments and not by their chemistry, these assertions require some further proof than the experiments so far afford, nevertheless the work is interesting in its suggestion.

The tar tumors and the transplantable

tumors doubtless will continue to contribute to the fund of knowledge about malignant disease. One feels, however, that the stimulation is far in excess of any natural irritation that could occur and that any natural defences of the animal are overwhelmed. Results, then, could readily be misconstrued.

Immunity.

Transplantable tumors have demonstrated that natural immunity may exist in certain animals. Transplanted tumors may retrogress after a period of growth. Following such a disappearance of the tumor at least 50 per cent. of these animals would be immune to further transplants of the same tumor, but not necessarily to other tumors. If one attempts to obtain immunity by injecting killed tumor cells then one is confronted with the development of cytotoxins against the cell injected as well as anti-bodies for the etiological agent. Lumsden (11, 12, 13), however, has developed a technique whereby he can cause the disappearance of malignant transplants. His first step is to obtain an anti-serum by injecting minced rat tumor into mice. The mouse is bled and the serum contains anti-bodies for rat tumor. Lumsden has transplants of the tumor growing in the feet of rats and when grown to a considerable size the leg of the rat is constricted and the anti-serum obtained from mice is injected in and about the tumor. The passive congestion of the tumor-bearing leg is maintained for several hours. Following such treatment the tumor disappears, and if there be tumors engrafted elsewhere in the body they too disappear. The animal is immune to further transplants. Then if serum is taken from this rat and used for tissue cultures, extraordinarily enough, rat tumor cells will grow in it. Superficially there are no anti-bodies for tumor present. However, if extravasated leucocytes (or an extract of them) from the same rat are added to the tissue culture, the tumor cells promptly succumb. This piece of work appears to be as significant as any so far carried out.

1. Canadian Art Movement.—Housser.
2. The Study of Experimental Cancer.—William Woglom.
3. Journal of Cancer Research.—April, 1926.
4. Journal of American Med. Assoc.—May 22, 1926.
5. Journal of American Med. Assoc.—Oct. 17, 1925.
6. Can. Lancet and Practitioner.—Nov., 1926.
7. Tissue Culture.—A Fischer, Copenhagen.
8. Studies of the Rockefeller Institute.—Last 10 years.
9. The Lancet.—July, 1925.
10. Journal of Cancer Research.—July, 1926.
11. Lancet.—Sept. 12, 1925.
12. Lancet.—July 17, 1926.
13. Lancet, July 15, 1927.
14. Jour. Exptl. Med.—1910, xii., 696.
15. Zeit. fur. Krebsforschung.—July 28, 1926.
16. Mueller, J. H.—Jour. Exptl. Med., Feb., 1927.
17. Kolmer et al.—Jour. Cancer Research.—April, 1926.

Liver Damage.*

II.—CLINICAL CONSIDERATIONS.

H. BORSOOK, Ph.D., 2T7.

The Functions of the Liver.

DAMAGE to the liver results in impairment of one or more of its functions.

The most sensitive function of the liver is its ability to destroy uric acid. As far as man is concerned, this is an inference only, from the conclusive results of experiments on animals. This inference is supported by clinical evidence. It is known that the liver suffers a reduction in all its functions when it is compelled to deal with large amounts of fat. Prof. Harding and his collaborators showed that the concentration of uric acid in the blood is increased on a high fat diet. This occurs also in star-

* Delivered before the A.O.A. Fraternity, March 21st, 1927. This is the second article under the heading "Liver Damage." The first, by Mr. J. Shier, appeared in the April issue, page 188.

vation, and probably in every instance of lipaemir. Kidney function tests showed that renal function was not impaired in the above experimental cases. High blood uric acid values are obtained, aside from nephritis, in gout, pre-eclampsia, eclampsia, arterial hypertension, lead poisoning, bichloride poisoning, acute infections, especially pneumonia, and in some cases of non-gouty arthritis. This finding in arthritis is interesting in view of the possible relationship, discussed below, between mild, long-standing liver damage, and the incidence of the degenerative diseases.

The function of the liver next impaired is the excretion of bilirubin. . This has been described in the previous paper.

The healthy liver also disposes of stercobilin which is absorbed from the intestine. In 1922 Whipple stated, "we know of no evidence of any sort to indicate that urobilin (formed from urobilogen, which is identical with stercobilin) or bile pigment are absorbed from the intestine. We believe that urobilin is formed in the liver, particularly in abnormal conditions of the biliary tract." A number of years before this von Muller had carried out the conclusive experiment of feeding bilirubin to a patient with complete mechanical obstruction of the common duct. After some hours urobilin appeared in the urine, from which it had previously been absent. This experiment was repeated in 1925 by Wallace and Diamond, with identical results. It has been demonstrated that numerous bacteria are capable of transforming bilirubin to stercoblin. The concentration of urobiligen is greater in the portal vein than in the jugular vein. When bacteria are introduced into the biliary ducts, then urobilogen is found there. Dr. Farquharson of the T.G.H., independently, demonstrated clinically that urobilogen is formed in the intestine from bile pigment, is in part absorbed and carried to the liver, where it is removed from the portal blood, if the liver is healthy, so that only minimal amounts appear in the urine. When the liver is damaged, the absorption of stercobilin from the portal blood is reduced, and consequently urobilogen appears in the urine in increased amounts.

The strategic position of the liver, between the intestinal canal and general blood stream, its compact structure and numerous Kupfer cells, confer upon it a pre-eminent importance in the protection of the whole organism against chemical and bacterial insults. Most of the metals are excreted in the bile. It has been shown that a given dose of a drug like atropine, hyoscine, or nicotine, is much more toxic when injected into the general blood stream than into the mesenteric vein. The liver is the chief organ concerned in the removal of insoluble and foreign particles from the blood stream. Bacteria are more readily removed by the liver than by any other tissue in the body. The increased tolerance of specifically immunized animals for a given organism is reflected in an increased phagocytic power of the liver for that organism. The liver plays an important role in the desensitization of foreign proteins. It has been shown that the liver of a sensitized animal can destroy the power of a given protein to produce an anaphylactic reaction. The detoxication of acetone bodies by glucose probably occurs in the liver. But the neutralization of indol and related toxins formed in the intestine, by converting them to ethereal sulphates, is not, in the dog at any rate, a specific function of the liver. Mann and Bollmann were unable to demonstrate any reduction in the rate of conjugation of ethereal sulphates in dogs from whom the liver had been removed. Similar results were obtained with benzoic acid, camphor compounds and salicylic acid.

The formation of bile acids may be considered as a detoxication of cholin by its combination with the amino acids glycocoll and taurine. This is a specific function of liver parenchyma.

Carbohydrate and protein metabolism is centered in the liver. Heptaic glycogen alone maintains the level of the blood sugar. Without it the blood sugar immediately falls and the animal dies. The intermediary metabolism of carbohydrate, the conversion of substances like dioxyacetone to glycogen, the group of workers associated with Dr. Campbell have shown, resides solely in the liver.

The deamination of amino acids and the formation of urea do not occur in the absence of the liver.

The whole intermediary metabolism, that

is all those processes by which the foodstuffs carried in the blood are split, reshaped and regrouped, rendered available for consumption, is centred, if it is not solely resident in the liver.

The desaturation of fatty acids preliminary to their oxidation is a hepatic function. But when the liver is handling fatty acids, all its other functions suffer. Uric acid increase in the blood and urine, the liver glycogen diminishes, its susceptibility to injury is increased. A possble explanation is suggested by the histological picture of the liver when it is metabolizing fat. When the fat globules are removed in fixing and staining the specimen, the remaining vacuoles, or holes rather, show that the fat seems to have usurped the place of the liver parenchyma. The latter appears compressed and reduced in amount.

The Causes of Liver Damage.

The following is a list of the causes of damage to the liver, that is the causes of demonstrable impairment of any or all of the functions outlined above, compiled from records of the Toronto General Hospital for 1926:

1. **Posons:** Arsenic, lead.
2. **Toxins:** Pneumonia, toxemias of pregnancy.
3. **Infections:** Any severe generalized infection, septicaemia, Weil's disease, catarrhal jaundice, cholecystitis, syphilis and cirrhosis.
4. **Tumours:** Secondary carcinoma of liver without obstruction, metastatic melanotic sarcoma of liver, terminal stage of myeloid leukemia .
5. **Cardio-vascular Disease:** Myocardial failure, anaemias.
6. **Degenerative Diseases:** Arteriosclerosis, with and without hypertension, emphysema, chronic bronchitis.
7. Physiological cholemia.
8. Mechanical obstruction.

The effect of an acute illness is illustrated in an observation by Drury and Rous. They found the 24-hour secretion of bile in an intubated dog to diminish from 160 c.c. to 10 c.c. during the course of an acute coryza.

There is a division of opinion in regard to the classification of catarrhal jaundice. One group considers the jaundice to be due to a cholangeitis causing obstruction in the ducts by plugs of mucous, desquamated epithelium, and inflammatory exudate. The other maintains that there is a suppression of secretion of bile on account of injury to liver parenchyma. The results of recent work are in favour of the latter view.

It is possible experimentally to produce a complete toxic suppression of bile, and in these cases careful examination of sections fails to disclose any material obstructing the ducts. Often there is a secretion in the ducts which is watery and colourless (the so-called "white bile").

The direct van den Bergh obtained in catarrhal jaundice, as pointed out in the previous paper, does not necessarily signify obstructive jaundice. The direct reaction is obtained in every moderate to severe case of hepatic jaundice. It is obtained in dogs after complete removal of the liver.

The presence of urobilogen in the urine in large amounts and its total absence in obstruction proves that bile enters the intestinal canal in the former case.

The course of "catarrhal" disease of the liver suggests that the lesion is in the liver parenchyma. Recovery is slow. Long after the stools are coloured, the van den Bergh, and the urobilogen in the urine remain high. On the whole, it appears that the disappearance of the colour from the stools in the course of toxic or infective injury to the liver is not due to obstruction in the ducts, but is rather a manifestation by the liver parenchyma of one of the cardinal symptoms of inflammation, viz., loss of function.

In mechanical obstructive jaundice there is a significant toxic element which persists for some time after the obstruction is removed. The serum of animals with an experimental obstructive jaundice, gives an indirect van den Bergh of 2 to 3 units prior to the appearance of the direct reaction. Drury and Rous found that tying off the ducts for only 24 hours so impaired the liver that it was unable to remove the dye, sodium indigotate from the blood, a property which the healthy liver possesses to a marked degree.

Walters and Parham reported a number of cases that developed hepatic insufficiency

2 to 8 days after removal of biliary obstruction.

In portal cirrhosis the injurious agent is probably a combination of the toxic and infective. The lesion until the end stages is in the portal circulation rather than in the liver parenchyma. Jaundice, consequently, indicating insufficiency of the liver parenchyma, appears only toward the end.

The so-called simple, familial physiological cholaemias comprise a group of individuals who show persistently an unaccountable indirect van den Bergh of 1 to 3 units.

Pathology.

The pathology is instructive in some of the commoner conditions. Myocardial failure is the cause of the jaundice most frequently seen. Here the intensity of the van den Bergh is paralleled by the amount of liver damage found at autopsy. The following three cases are typical:

1. Age 65. Liver not enlarged, van den Bergh 1.8. There was intense congestion in the central vein area; but no necrosis. The cords were stained palely and were infiltrated with fat. The nuclei were pyknotic. The sinusoids were dilated and contained a small amount of debris. There was a slight increase of connective tissue.

2. Age 56. A history going back 5 years. The liver was not palpable. The van den Bergh was 3 units and positive direct.

There was marked central vein necrosis involving about 1/3 of each lobule. The cells bordering upon the necrotic areas were compressed and showed degenerative changes similar to those described in the first case. The cells in the portal areas appeared normal.

3. 19 years—rheumatic myocardial disease with mitral stenosis and aortic insufficiency. The history went back 10 years. There was a terminal influenzal bronchopneumonia. The liver was palpable an inch below the costal margin. The van den Bergh was 11.3 units. The central necrosis involved about ¾ of each lobule, with all the remaining cells showing degeneration. The central vein areas and the sinusoids were engorged with red cells.

These examples emphasize that in every case of myocardial failure, and especially where there is visible jaundice, there is the complication, which at the time may be as grave as the myocardial failure, of advanced hepatic failure.

A similar central vein necrosis is found in arsenic and in chloroform poisoning and in severe anaemas. The smilarity of the lesions in the latter cases to those described in myocardial failure has suggested to some that the essential toxic agent to the liver in the cardio-vascular disorders may be anoxoemia. The deepening of the jaundice after pulmonary infarction has been attributed to this factor.

In acute yellow atrophy from arsenic poisoning the liver is shrunken and tender, and the van den Bergh very high. In one case, 3 days before death it was 77 units. The liver lobules were all smashed up. Only remnants remained. These remaining cells and the bile ducts were bile-stained. Yet even here, there were signs of regeneration in the growth of groups of cells out from the bile ducts.

The effect of mechanical obstruction is shown in a case who died of carcinoma of the stomach, but in whom no secondaries were found in the liver. There was no definite destruction of liver tissue; but the cytoplasm of the polygonal cells throughout was dull and hazy. The cells were swollen and contained a good deal of bile pigment. Their nuclei varied in size and staining. There was a yellowish green zone about the portal areas.

In a fatal case of pneumonia in which there was cyanosis and jaundice, there was a uniform cloudy swelling throughout the liver. There seemed to be no healthy gland whatsoever, but there was no necrosis. The picture contrasts sharply with that found in the anaemias and in myocardial failure; and, it seems, definitely excludes anoxoemia as the cause of the jaundice.

Here.

An example of a severe infectious jaundice is the case of Weil's disease reported by Dr. Bates. The lobular formation was indistinct, the liver cords were swollen and jumbled; and in some instances the individual liver cells appeared separated from each other. The nuclei showed the usual degen-

erative changes. The central vein areas were congested, the sinusoids were widened, compressing the liver cords. Fatty infiltration, areas of hemorrhage, and an increased amount of fibrous tissue in all portal areas, were prominent features.

No examples of catarrhal jaundice are available in our department of pathology. Regarding the pathology of this condition Small states:

"In cases of toxic or infectious jaundice the initial damage occurs in the polygonal hepatic cells themselves, all degrees of pathological change from simple cloudy swelling to actual necrosis being observed. The portal spaces and biliary capillaries are only secondarily affected.

"I have had the opportunity of studying several cases of toxic jaundice of unknown origin in which no obstruction of the bile ducts could be demonstrated. In these cases the development of definite cirrhosis was confirmed by biopsy made at time of exploration."

In regard to cirrhosis McNee and others have suggested that all the changes observed in toxic and infective diseases of the liver, ranging from simple hepatitis to acute yellow atrophy and cirrhosis of high grade are all part of the same pathological process. Continental physicians, notably Eppinger, have considered the relation of the reticulo-endothelial system to hepatic disease. They have assembled the cirrhosis associated with splenomegaly, Banti's disease and certain types of biliary cirrhoses, in a group of liver-spleen diseases. Improvement following splenectomy has been explained on the basis of removal of functional overload of toxins elaborated by the reticulo-endothelial cells in the spleen.

Symptoms of Liver Damage.

Symptoms of liver damage manifest themselves mainly in three systems. There are dry, furred tongues, marked loss of appetite, flatulence, nausea, vomiting and constipation. The patient tires easily because of muscular weakness involving the myocardial as well as the skeletal muscles. The nervous symptoms are malaise, languor and mental depression, or restlessness and irritability, progressing in severe cases to somnolence, stupor and coma, or delirium and mania.

The two outstanding symptoms of catarrhal jaundice are the total absence of appetite, and the profound languor, with the loss of all desire for activity of any kind.

A prominent symptom of liver disease is the tendency to hemorrhage, into the skin, mucous membranes and solid organs.

Another characteristic is the latent period between the incidence of the toxic factor and the appearance of symptoms. In chloroform poisoning in dogs, symptoms frequently do not appear until 24 hours after the administration of the chloroform. Mann and Bollman found repeatedly that dogs with an experimentally reduced amount of hepatic tissue died suddenly several days after phenoltetrachlorphthalein tests had been carried out upon them. Clinically there is the interval between the gastro-intestinal symptoms and the appearance of jaundice in catarrhal jaundice and in Weil's disease. The liability of patients receiving arsenic treatment to exhibit marked symptoms suddenly after a long course of treatment, some time after the treatment has stopped, is well known. In the cases of hepatic failure after cholecystectomy, reported by Walters and Parham, symptoms appeared suddenly 2 to 8 days after operation.

Liver Function Tests.

These are based upon known functions of the liver. They meet with the difficulty that an enormous amount of the liver must be incapacitated, between 70 and 90 per cent., before any deficiency of function can be detected with any of the present tests. The so-called liver function tests would be more correctly named tests for liver damage. For instance, in an accident in which the whole of the right lobe of the liver was seen, at operation, to be involved, the phenoltetrachlorphthalein, and fructose tolerance tests were normal, and there was a van den Bergh of only 3 units.

An additional difficulty with most of the tests now employed is the intrusion of the kidney.

To-day there are only two reliable methods for measuring liver damage, the estimation of the bilirubin in the plasma

by the van den Bergh method, and the estimation of the urobilogen of the urine.

The tests based upon the functions of the liver associated with carbohydrate metabolism, the fructose tolerance test, and with protein metabolism, the ratio of urea nitrogen to the total non-protein nitrogen of the blood, are of little value because these functions are most resistant to injury. They are only slightly impaired in cases of most severe damage to the liver.

A test from which a good deal was expected at one time was the phenoltetrachlorphthalein test. The underlying principle is that dye injected into the blood stream is quickly excreted by a healthy liver into the bile, so that 15 minutes after injection only 5 to 7 per cent. of the injected dye is found in the blood stream. In disease excretion is supposed to be slower and correspondingly larger amounts are expected in the plasma. The test has been a disappointment and has been abandoned almost everywhere except at the Mayo Institute. There, a group of workers, which includes Rowntree, found a parallel between the retention of the dye in the blood and the van den Bergh in the cases of severe jaundice. They believe in its value in these cases in following the course of recovery. They believe also that the dye test is more sensitive than the van den Bergh in cases of cirrhosis and in secondary carcinoma of the liver.

Here and elsewhere the dye test has been found less sensitive and less reliable than the van den Bergh. Another unsatisfactory feature is that the veins of the patient are punctured four times in two hours with the dye test, while only one sample of blood is removed for the van den Bergh.

This test has definitely supplanted the dye tests. The principles, interpretation and details have been presented in the previous paper. As stated earlier, in the dog, next after the destruction of uric acid, the excretion of bile pigment is the function of the liver most easily impaired.

Without this test the group designated as "simple" or "physiological cholaemia" escape attention. These cases are interesting because we may have a clue in them to the nature of the predisposition to the degenerative diseases of later life. In the routine examination of a number of normal individuals, the few whose sera gave van den Bergh's of 1 to 3 units did not justify the title "physiological" cholaemia. They were not without symptoms. They did not feel well, nor did they give the impression of being perfectly healthy, Excluding increased haemolysis, the van den Bergh test bears an analogous relation to hepatic function as the non-protein nitrogen does to renal function. A non-protein nitrogen of 40-50 in an individual without symptoms would hardly be dismissed as insignificant or be designated as an idiopathic or physiologically high non-protein nitrogen. There seems little justification for considering a van den Bergh of 1 to 3 units in a patient without definite symptoms, as such, in view of a normal value of 0.3 to 0.5 of a unit. It is interesting in this connection that a number of cases diagnosed clinically as hypertension, arteriosclerosis, emphysema, chronic bronchitis, gave van den Bergh's of 1 to 3 units. When 70 per cent. of the liver must be removed in a dog before the bilirubin of his plasma is increased above normal, a value in the human, two to six times the normal can hardly be insignificant. Van den Bergh observed in some cases of physiological cholaemia an increased urobilin in the urine and a slightly enlarged spleen.

The van den Bergh test provides also an accurate method for estimating the severity and for following the course of hepatic disease.

In lead poisoning most of the cases gave an indirect reaction and a value of 1 unit. This, in all likelihood, was due to increased haemolysis and not to liver damage. All these cases were more or less anaemic. A few gave the direct reaction, and values from 3 to 7 units. In these cases the liver by our criterion must have been moderately severely damaged.

In arsenic poisoning van den Bergh's as high as 30 units occur. In one such case this test showed that the liver did not completely recover for months after symptoms had disappeared. On Dec. 17 the van den Bergh was direct, and 30 units. On July 2 there was still a van den Bergh of 2-5 units. Another milder case showed on Dec. 28, 4.6 units. But a month later it was still 1.8 units. The typical course in these cases of

arsenical jaundice is a quick reduction of the van den Bergh with suitable treatment; but the normal value is not attained for months. No data are available, but it may turn out that it never returns to normal in these cases, which would indicate that permanent damage had been inflicted upon the liver.

As a rule with the high van den Bergh values in these and other types of cases there were also high non-protein nitrogen, with values ranging from 80 to over 100 and low chlorides below 0.4. It is not possible to interpret these findings without definite information regarding the condition of the kidneys.

The highest van den Bergh recorded in a case of pneumonia was 11.0 units. Generally it was highest when the symptoms were worst, and it declined with improvement. All sera with concentrations of 3 units or more also gave the direct reaction. Below this only the indirect was obtained. Unlike the arsenical cases, once improvement set in, there was a speedy recovery. A typical case gave on May 23 a value of 7.2 units. Eight days later it was practically normal. Of eight cases of pneumonia with visible jaundice, two died. The common statement that jaundice is of grave prognostic significance in pneumonia was not substantiated in this short series.

As an example of another toxemia, an eclamptic patient gave a direct reaction, with a value of 2 units.

The highest Van den Bergh values were obtained in two cases of Weil's disease. One gave 85 units, the other 77 units. Here, as in the arsenical cases, with improvement of symptoms there was an initial rapid decline of the bilirubinaemia, followed by a long persistence of a low value. The one case gave 85 units on June 11; on July 5, 2 units; but on Aug. 2 there were still 1.6 units. The other case ran a similar course. Here also, at the height of the jaundice there were high non-protein nitrogen and low chloride values.

The effect of a severe focus of infection is shown in a case where the diagnosis rested between encephalitis and brain abcess. There was a direct reaction and a concentration of 2.1 units. In a case of acute otitis media due to streptococcus haemolyticus there was a van den Bergh of 1.0 unit.

Very high values are found in catarrhal jaundice. Here again the course of recovery is similar to that in the cases of arsenical poisoning and Weil's disease. The following figures present a typical case:

Sept.	3.—Direct	31.2
	7	12
	10	6
	16	4.8
	20	4.7
	23	4.0
	27	3.2
Oct.	4	1.6

Most cases of chronic cholecystitis give normal values. According to Graham, who supports his conclusions with a number of direct observations, in every case of cholecystitis there is some hepatitis. Normal Van den Bergh values in these cases must be taken to indicate that the degree of liver involvement is not great. An occasional case gives a high value. There was one case with over 6 units. The subsequent course of this type of case would be interesting, but no data are available.

In two cases of cirrhosis the Van den Bergh was direct, and the values were 1.6 and 1.8. In both of these cases there was a large amount of urobilin, out of all proportion to the Van den Bergh. The location of the lesion here in the portal circulation rather than in the liver parenchyma probably accounts for the discrepancy between the results with these two tests which in all other cases run parallel.

The most common cause of jaundice is myocardial failure. Nearly every case shows some increase in the Van den Bergh. In some severe cases values as high as 30 units were found. As might be expected, the highest values were abtained in cases of mitral stenosis. Viewing all the cases together, the size of the liver as determined clinically, did not correspond to the height of the Van den Bergh. But in the progress of any one case, the size of the liver and the value of the Van den Bergh did run roughly parallel. There was no correspondence between the presence or absence of cyanosis

or oedema, and the Van den Bergh. In myocardial failure the appearance of visible jaundice and its progressive deepening is of the gravest prognostic portent. Usually death soon supervenes.

The workers at the Mayo Institute entertained the hope that the dye test might prove of value in the diagnosis of secondary carcinoma of the liver in the absence of visible jaundice. A priori it is hardly to be expected that one or two metastatic nodules can sufficiently impair the function of an organ as large as the liver, so that they might be detected by any of the modern tests, which reveal only fairly severe grades of liver damage. The available data here do not encourage the hope of early diagnosis of metastasis in the liver by the Van den Bergh test. It would be surprising if dye tests proved to be any more sensitive.

A test which seems to be as sensitive as the Van den Bergh is the estimation of the urobilogen in the urine. The principle underlying this test has been described. The test is carried out on a small amount of fresh urine. It is essential that the urine be fresh, because urobilogen is converted to urobilin on exposure. A red colour develops in the urine on the addition of Ehrlich's aldehyde reagent. The specimen is diluted down until the colour disappears. The urine of normal individuals requires dilution from 10 to 20 times.

In catarrhal jaundice the dilution required may be as high as 3,000. Urobilogen is not present in the urine in all stages of this disease; but it invariably makes its appearance at one or another time during its course. Its total disappearance is indicative of restoration of liver function in spite of the fact that jaundice may be still present.

In subacute conditions associated with jaundice the urinary urobilogen is usually increased. In chronic liver disease the value may be normal, as with the van den Bergh test. Similar to the van den Bergh test also, urobilogen increases with increased haemolysis and correspondingly similar precautions must be taken in interpretation of results.

The following table indicates the general parallelism between the results with the urobilogen and Van den Bergh tests.

Case.	V.d.B. units.	Urobilogen
Catarrhal J. 2½	20	1:75, 1:250
Cholangeitis, followed by liver abscess.	6	1:200
Chronic cholelithiasis and diabetes	2	1:50
Chronic endocarditis and enlarged liver		1:30
Myocardial Failure..		1:1,500
Primary Ca. of liver.		1:150, 1:300
Ca. of gastro-intestine No secondaries ..		Normal.

These two tests are the most valuable laboratory aids available to-day in the diagnosis, and prognosis of hepatic diseases. They permit the recognition of injury to the liver before the appearance of visible jaundice which indicates severe liver damage. Following biliary colic the bilirubin of the serum is always increased, even though there may not be visible jaundice. With these tests it should be possible, it seems, to distinguish between toxemias of pregnancy of renal and hepatic origin, not, as heretofore, by the course of the disturbance after it has passed, but in its incipient stages. In the special treatment clinic with routine van den Bergh tests in all cases, mild degrees of toxic injury to the liver are recognized, treatment is stopped, and as a result, visible jaundice due to arsenical poisoning of the liver has been completely prevented.

The accuracy with which these tests permit us to follow the course of recovery of hepatic disease has been described.. The comparison seems not far-fetched of the long persistence of a Van den Bergh of 1 or 2 units, and increased urobilogen, after toxic hepatic jaundice, with the slow disappearance of small numbers of red cells from the urine after acute nephritis.

In the treatment of liver disease the most important therapeutic agent is carbohydrate. Opie and Alford showed years ago that the ability of an animal to withstand chloroform poisoning was definitely dependent upon the glycogen content of the liver cell. It is possible that the notorious susceptibility of diabetics to infection lies in the low glycogen content of the livers of these individuals. The efficacy of glucose

in treating severe liver damage has long been established. In all cases of coma of hepatic origin glucose is given intravenously. In the treatment of arsenical poisoning carbohydrate, intravenous glucose if necessary, is employed in addition to sodium thiosulphate. Mann found that feeding glucose greatly increased the period of survival of animals after induction of obstructive jaundice. High carbohydrate diet is clearly indicated in the pre and post-operative periods of cases of biliary obstruction.

Fats are definitely contra-indicated. In severe cases they should be completely absent. In milder cases fats are profitably reduced to the minimum amounts short of rendering the diet unpalatable.

In severe cases proteins are best reduced to the amount just sufficient for the maintenance of nitrogen equilibrium, in an adult about 50 gm. a day. In mild and chronic cases this amount may be increased; but a high protein diet is contra-indicated.

The traditional bad reputation of purine-containing foods has been justified. As pointed out earlier, the destruction of uric acid is the function of the liver most easily impaired. All forms of flesh, liver, thymus and pancreas contain relatively large amounts of purines and should be avoided. Peas and spinach are also in this category. Almost all other vegetables, white bread, cereals, milk and milk products, and eggs, on the other hand, are quite safe.

In view of the probably impaired detoxicating function of the liver the bowel should be kept clear. Space does not permit discussion of non-surgical biliary drainage in liver disease.

In conclusion it should be pointed out that the consequences of disease of the liver have been interpreted in terms only of impairment of known functions of liver. Certainly not all the functions of the liver are yet discovered. No attempt has been made to identify any perversion of liver function due to disease, with the resulting production of toxic substances; though the acetone bodies may possibly be considered as such. It is possible that interference with as yet unidentified functions, toxic substances, and nervous disturbances resulting from perverted metabolism may be responsible for signs and symptoms, which will permit, when their significance is recognized, detection of liver damage, even earlier than is now possible with the Van den Bergh and urobilogen tests.

Practically all the clinical data referring to cases in the Toronto General Hospital, quoted here, were compiled from the original observations of Dr. R. F. Farquharson. The author wishes to thank him for permission to use these, and for material assistance in the preparation of this paper.

Gonorrhoea in the Female.

F. J. O'LEARY, M.B.

ALTHOUGH there is some controversy as to the role played by the various pus-producing organisms in infections of the female genital tract, there is no doubt that the gonococci causes the most variegated and extensive alterations and that it produces most serious effects in the health and life of the individual, thus exerting a baneful influence on the welfare of the nation. On this account, we are disregarding the tuberculosis, syphilitic and chancroidal infections, also those caused by non-specific organisms, and are dealing only with acute and chronic gonorrhoeal infection.

Unlike most other bacteria, the gonococci require no portal of entrance, no local lesion. Implanted on an intact mucous membrane, it penetrates readily through the epithelial surface and there proliferates rapidly. As infection occurs usually during sexual intercourse, the organisms are deposited simultaneously on the urinary meatus, and the external os of the cervix. After three or four days an inflammation is produced with the cardinal signs, heat, swelling, redness and pain, the natural results of tissue reaction.

The migration of leucocytes and hyper-

aemia causes a sensation of uncomfortable dryness—the pressing of the leucocytes through the epithelium marks the beginning of a purulent secretion. Cell proliferation is more active and pressing on the nerve endings, causes pain.

When the urethra is involved, the mucosa is reddened and swollen and a greenish yellow pus oozes from the meatus. Urination is painful, frequency and urgency are present. Every urethritis is not gonorrhoeal, but when the symptoms are marked the gonococci can usually be found in pure culture.

The first sign of infection of the cervix is not nearly so stormy as in the urethra because the former is relatively devoid of sensory nerve endings. Yet the acute swelling impresses itself on the patient's consciousness by a sense of weight and fullness, and the profuse muco-purulent discharge pouring over the vagina and vulva irritates those sensitive surfaces and infects the Bartholin gland with or without abscess formation. Occasionally the discharge is so irritating that the tissue reacts in the form of condylomata acuminata or venereal warts. Usually after a few weeks the general inflammation subsides spontaneously, the vaginitis disappears and the infecton remains limited to its original sites.

The cervix is the great stronghold of the gonococci. The squamous cell epithelium in the adult vagina is resistant to the infection, but it easily burrows through the columnar epithelium of the endocervix and thus finds its way into the racemose glands forming the bulk of the cervix. As these glands become full of inflammatory products and their ducts are pressed upon by inflammatory infiltration, drainage is interfered with and retention cysts result.

The diagnosis of female gonorrhoea is probably based more on clinical than bacteriological findings. In the acute stage the organisms are readily found, but as it becomes subacute they bury themselves in the tissues and a series of slides may prove negative. What concerns us most in connection with gonorrhoea is the treatment. It has been said that gonorrhoea in the male is overtreated and in the female undertreated. The many contradictory forms of treatment testifies to the uselessness of many of them and to the impossibility of using routine methods in all cases.

General treatment demands absolute rest in bed during the acute stage and even when chronic the patient should take to bed during the menstrual period. Heavy work is forbidden, and also sexual intercourse. The diet should be bland and bowel action regulated, and alcoholic drinks prohibited.

For gonorrhoeal urethritis the following recommendations are made:

1. Warm compresses of acetate of lead to relieve the painful swelling.
2. Encourage diuresis with plenty of water and alkaline salts. Urotropin is contraindicated on account of its irritating action on mucous membrane.
3. Injections of argyrol or protargol into the urethra with an eye dropper.

Chronic urethritis requires dilation with a Kelly endoscope and application of silver nitrate solution to the mucous membrane. Skene's glands, lying beneath the urethral floor, with the entrance to the ducts just inside the urinary meatus, usually harbor the germs for long periods and act as foci of reinfection. They can be exposed by pressure with an ordinary hairpin after retracting the anterior urethral wall. Injections of silver nitrate into the duct are recommended, but better still the duct is slit open or burned out with a pointed electric cautery.

Infection of the Bartholin gland is treated by incision if there is pus formation. If only the duct is involved, injection with a blunt needle of silver nitrate solution is required. If a chronic infection of the gland persists, surgical removal or thorough cauterization is demanded to utterly destroy one of the chief hiding-places of the gonococci.

As mentioned before, warts are caused by an irritating discharge flowing over the vagina and vulva. They may be destroyed by an electric cautery or nipped off with scissors and the bases cauterized. If very extensive, X-ray or radium in small doses is considered an absolute specific.

Now we come to the treatment of cervicitis and endocervicitis of gonorrhoeal ori-

gin and I will enumerate some of the methods that have proved efficacious in different clinics. Most authorities agree that the best policy is to try and assist nature by gentle measures rather than try to eliminate the disease by aggressive action. Even douches are forbidden by some in the acute stage because they lack curatory value and because of the danger of forcing the infection higher up.

The time-honoured styptics and antiseptics are giving way to mercurochrome and other non-irritating, but penetrating drugs. Mercurochrome is universally used in strengths of 2 to 5 per cent., but Brady of Johns Hopkins Hospital is using 10 to 20 per cent. solution with gratifying results. No ill effects are noted from this concentrated form. It must be remembered that fresh solutions should be made every few days. The usual procedure is to clear the cervical canal of its secretion with peroxide or solution of soda bicarbonate, it is dried by cotton on an applicator, then mercurochrome solution applied within the canal to the cervix and over the vaginal walls. These treatments should be repeated every second day if possible.

Albrecht and French recommend douches of chloride of zinc, one or two a day, intra cervical applications of formalin every three days and the use of cervical suppositories of protargol.

Clarke of Philadelphia first clears the cervix and applies Lugol's solution of iodine and inserts boroglycerate and iodine tampons against the cervix.

In some clinics, yeast is employed in the form of a powder which is introduced into the vagina with a blower, depending on its bacteriacidal properties to overcome the gonococci.

Corbus and O'Connor are using a method of treatment by heat on the assumption that gonococci are killed by relatively low degrees of heat. An electrode is placed in the cervical canal and the temperature raised to 117 F. for twenty minutes at a time. This is repeated every seven to ten days. This method is employed only in chronic conditions.

Spuman is a name given to a mixture of various antiseptics mixed with tartaric acid and soda bicarbonate. When introduced into the vagina, carbon dioxide gas is released, distending the vagina and forcing the antiseptic into the folds of the mucosa.

Gellhorn of St. Louis follows three methods, alone or in combination:

1. Injection of 1 per cent. solution of methylene blue into the cervical tissue in hopes of reaching the organisms buried in the glands. This is done with an ordinary hypodermic syringe—the needle is inserted at the four points of the compass and as it is withdrawn, 1 to 2 c.c. of solution is injected. This is repeated twice a week and cures have been reported after six treatments.

2. Heat penetration after the method of Corbus and O'Corror.

3. Nassauer's powder treatment—more valuable in acute than chronic cases. A mixture of Fuller's earth and baking soda is used. This interferes with the growth of bacteria by robbing them of their media, and it protects the vagina from irritating discharge. The powder may be introduced with a spoon through a speculm and held in place by a tampon, or, the patient herself may use a special siccator.

Within the past few years, thermo-cauterization has become a very popular method of treatment of chronic infections of the cervix, especially accompanying lacerations with eversion of the lips or erosion. Formerly, the tendency was to make deep radical incisions through the mucosa with a Paquelin cautery, but Dickinson has shown us the advantage of using the electro-cautery of the rhinologist. His technique consists in making four linear strokes at the four points of the compass from the internal to the external as, carrying them over the eroded lips. The diseased tissue is thus destroyed and when healing of the tiny gutters occurs, the shrinkage and inrolling tend to correct the inversion of the lips. Treatment is repeated in two weeks, stroking the areas between the lines of scarred tissue.

In the treatment of cystic cervices, the cysts are destroyed by stab incision with the cautery. This method is a real boon,

and takes care of many cases of chronic cervicitis with a voluminous mucous catarrh of the canal that otherwise would necessitate amputation. It is painless and can be carried out as an office procedure. Cauterization must not be done in the acute or subacute stage of endocervitis, nor if there is any tubal involvement.

Amputation of the cervix always remains as a last resort for obstinate cases of chronic endocervitis, especially where extensive laceration and erosion exist. The most popular and safest method is that of tracheloplasty originated by Sturndorf. By this method the diseased area is outlined with a scalpel, a cone-shaped piece of tissue reaching from the internal os to the vaginal portion of the cervix, is removed. This takes away the gland bearing portion of the cervix and leaves behind a cuff of healthy muscle lined with vaginal mucous membrane. The great advantage of it is its thoroughness and the fact that the retractive qualities of the cervix are not interfered with during subsequent labour. According to Sturndorf, a diseased cervix is responsible for more pelvic distress and backache than generally supposed, and there is a constant migration of toxins along the lymphatics to the cellular tissue of the pelvis. This trachtloplasty then does more than eradicate an obstinate discharge—it removes the source of many pelvic symptoms.

This is a brief outline of a few of the many methods used in the treatment of gonorrheal infection of the cervix. Our faith in these is best shown by the methods used in our own practice. In the public health clinic at St. Michael's Hospital, where forty to fifty women are constantly under treatment, we depend on the following routine:

1. Rest in bed and general hygienic measures during the acute stage.

2. Frequent intercervical applications of 5 per cent. mercurochrome as often as four to six times a week if possible, after clearing away the discharge with alkaline solution.

3. Instillation of 1 per cent. methylene blue into the cervical tissue.

4. Insufflation or packing the vagina with a mixture of Keotin and baking soda, two to three times a week.

5. Alkaline douches as cleansing agents only.

6. The electro cautery in chronic cases with no tubal involvement.

7. Sturndorf tracheloplasty of hypertrophied cystic cervices of long standing with lacerations or erosions.

8. All affected parts, urethra, cervix and Bartholin gland, must be treated simultaneously to prevent reinfection one to another. Generally speaking, not one of the methods discussed is absolutely certain of results. The condition demands a great deal of perseverance on the part of the physician and patient, and the practitioner may have to change from one method to another in the course of his treatment.

Just a word as to when the patient is cured. That is a difficult question to answer. Negative smears are an uncertain guide. I have seen six smears taken carefully, show absence of gonococci and the seventh was positive. To be honest with one's self and the patient, smears should be taken after provocative measures:

(1) After menstruation.
(2) Hot Sitz bath.
(3) Injection of 5 per cent. silver nitrate into urethra and cervical canal.
(4) Subcutaneous injection of 50 to 100 million of gonococci vaccine.
(5) Sexual intercourse with condom.

Sometimes recrudescences of the disease are observed months and years after the patient has been pronounced cured. Bacteriological examinations should be made from time to time and finally the possibility of re-infection should not be left out of consideration.

The Functions of the Spleen.

A. FINE, 3T0.

THE spleen until recently well deserved the name that Galen had applied to it, the "Mysterious Organ." It has attracted attention from very early times and the ancients knew that it could be removed without fatal results. Its excision was often performed by the Greeks, who thought that they could render their athletes speedier because of a mistaken idea that the giraffe possessed no spleen, a fact which they believed was the reason for the giraffe's speed. That an improvement followed removal is not to be wondered at, for those athletes who had suffered from malaria often had enlarged spleens, which were the breeding-places for micro organisms. Their results have been unexpectedly confirmed by Marht and Finesilver, who found that the speed of rats following splenectomy was much improved, but no explanation has been offered.

While the spleen is still a mysterious organ as regards some of its functions, yet to-day we know definitely that it is concerned with blood cell destruction and blood cell formation, that it has a controllable reservoir system and so forth.

The favorite method of attack has been that of splenectomy since the operation may be performed without fatal consequences. Results have not been conclusive in some cases, for investigators have not taken into account several factors, such as the relation of the spleen to body weight, varying from 25 per cent. in the dog to 0.5 per cent. in rabbits and cats, the presence of accessory spleens, and moreover, age is an important factor, for Gross has shown that the spleen is most active in the young, and he considers it largely inactive in man after the age of 40. Muckhard's work seems to confirm this, for in his experiments splenectomized kittens usually lost weight and died young.

Histology and Anatomy of the Spleen.

The spleen is divided by means of connective tissue partitions or trabeculae into lobules, which are in turn further subdivided by prolongations of the trabeculae, which form the connective tissue framework of the spleen. The branches of the splenic artery entering at the hilum and running some distance within the trabeculae in company with the vein, break up into smaller branches which enter the centre of a lobule and given off branches to its subdivisions. Now the artery on leaving the trabeculae, carries with it some connective tissue which with the adventitia from an envelope of considerable thickness. Within these envelopes lie accumulations of lymphoid tissue which surround the artery and are known as splenic nodules or malphigian bodies. During its passage through the nodule, the artery gives off capillaries, which may end in the nodule or pass directly into a venous sinus.

The terminal twigs of the artery known as pulp arterioles after repeated branching give rise to capillaries with quite thick walls. These capillaries may pass directly into a venous sinus and thence to the vein or they may lose their thick walls, the blood escaping into the splenic pulp which thus becomes infiltrated with great numbers of erythrocytes. It is apparent, therefore, that while one part of the blood actually passes into the spleen pulp, another portion passes by a closed route and under the usual conditions from artery to vein, without mingling with the lymphoid elements of the pulp and that these controllable shunts offer apportunities for storage. In the pulp are many types of cells, blood cells which have left the vascular channels, such as erythrocytes lymphocytes, polymorphonuclears, platelets and in addition, the pulp cells or splenocytes which are closely related to the endothelial cells of the venous sinuses and the cells of the supporting reticulum, the latter three types making up what is known as the reticulo-endothelial system. These reticulo-endothelial cells which are white widely scattered, are found in the liver, bone-marrow, etc., and possesses marked phagocytic powers being intimately concerned with the removal of effete red

corpulcles, bacteria and other foreign matter.

Now as regards the several functions of the spleen the first one to be dealt with is the relation of the spleen to blood formation. That the spleen does manufacture erythrocytes and leucocytes infetal life is beyond question. The mesamoeboids, the first formed corpuscles, which form the reds or the white and reds as some think, increase by division in the interior of the embryo in regions where the circulation is sluggish and allows of the accumulation of blood cells. After birth, the hematopoietic function of the spleen is limited only to the white corpuscles while the bone-marrow is the site of formation of both white and red corpuscles. However, in case of severe clinical or experimental anemias or extensive destruction to the bone-marrow, post mortem examination has shown the presence of tissue indistinguishable from bone-marrow and also cells which are forerunners of the erythrocytes.

Regarding the formation of lympochytes this probably takes place throughout life for the lymphoid tissue of the spleen constitutes one of the two chief sites of lymphoid tissue in the body, while Downey and Weidenrich found that lymphocytes are supplied to the circulation directly by the Malphigian bodies and the pulp, for lymph channels are absent from the interior.

The effects of splenectomy have been studied very extensively by Krumbhaar and many others who found among other things that a severe anemia occurs following the operation and lasts longer in the case of young animals. The question is now as to the cause of this transient anemia. Injection of splenic extract brings about immediate relief and moreover, the absence of immature corpuscles has led Krumbhaar and Leake to believe that the anemia is not due to an excessive breakdown of red corpuscles, but rather is due to the fact that the spleen exercises a stimulating effect on the bone-marrow. If an Eck fistula be made in a dog or the splenic vein implanted into the inferior vena cava, either of these operations being substituted for splenectomy, the same sort of anemia is produced, showing that the action of this extract, if it exists, depends on it traversing the portal circulation and the liver.

Splenectomy has an influence on the quality of the red cells, all observers agreeing that the corpuscles become more resistant to hypotonic solutions, i.e., their fragility is decreased. This is undoubtedly a factor in the beneficial effect of splenectomy in certain anemias and also lessens considerably the amount of jaundice following the administration of hemolytic agents. As to the cause and significance, it might be that the spleen can excrete some sort of agent which renders the corpuscles less resistant to action, but the evidence is too scanty at present to decide on any definite conclusions.

Relation of the Spleen to Blood Destruction.

That the spleen is the graveyard of the blood corpuscles was conclusively shown by Kolliker and Ponnfield, who were able to note the phagocytosis of erythrocytes and also foreign matter, which is due of course to the activity of the reticulo endothelial system. Blood destruction takes place elsewhere in the body owing to the widespread distribution of this system. Linked up with this is the statement made above, viz., that the spleen renders corpuscles more fragile. Recent observations by Mann and his coworkers have actually shown an increase in bile pigment in the splenic vein over that in the artery showing that the spleen does manufacture bilirubin out of the hemoglobin from those corpuscles destroyed.

In splenectomized dogs, Henn found that the blood-platelet count was increased and the coagulation time shortened, this seeming to suggest that the spleen may actually destroy blood-platelets or it may have an inhibitory influence on the megakaryocytes in the bone-marrow, but this again is still an open question.

Clinically, erythrocyte destruction may become dangerously active in certain diseases. For instance in hemolytic jaundice, removal of the spleen is followed by a reduction in blood destruction and in Banti's disease, splenectomy results in a definite cure. In pernicious anemia only a temporary improvement follows splenectomy, the other members of the reticulo indothelial

system taking its place. The answer as to why there should be a difference in these diseases, following splenectomy, may shed some light on the cause of pernicious anemia.

The Reservoir Function of the Spleen.

The fact that the spleen can materially influence the amount of hemoglobin in the circulation, that it can act as a controllable reservoir has been quite clearly proven by Barcroft of the University of Cambridge. His attention was first attracted towards this matter, while travelling towards South America. During his voyage, while doing some experiments on blood volume, he noticed that the hemoglobin content of the body arose as the temperature of the surrounding air increased, and vice versa. Thinking that temperature changes were responsible, on returning home, two volunteer workers were placed in the glass room of the Cambridge Laboratory and the temperatures raised and lowered. The variations in blood volume were exactly as they had taken place on board ship and temperature changes were clearly the cause. This is due of course to the fact that the vessels of the skin dilate and they naturally require more blood which comes from the interior. Now as the interior may need the blood, we see at once the necessity for a store of hemoglobin somewhere.

There was no evidence of increase of bone-marrow function, and moreover, there was no evidence of increase of immature erythrocytes. Barcroft suspected therefore that the body contained a hidden store of hemoglobin which might be used in the case of need. There is only one organ in the body of considerable size, the spleen, which is packed with corpuscles which are out of the general circulation, so much so indeed that there is a lag of 20 minutes between the time at which the blood contains a certain percentage of co-hemoglobin and the time at which the erythrocytes in the spleen pulp acquire the same percentage.

When one considers the small size of the spleen and its weight, only 200 g., it hardly seems credible that such an organ could possibly influence the amount of blood in the circulation, yet one must bear in mind this fact, that it is always a post mortem spleen that is being examined. The next point to be cleared up was the size of the spleen in normal animals. A very ingenious experiment was devised. A cat was opened and metal clips were attached to various points on the spleen. It was now photographed by X-Ray before, during and after, the experiment changes in volume being estimated by the changed position of the clips. The cat was killed and just before the removal of the spleen, it was again photographed. The spleen was now removed, weighed, and one could now calculate the weight of the organ in the animal.

The results obtained showed that the spleen was 2 to 4 times heavier in the living than in the dead animal and that it lost 10 to 20 g. in weight. Since the blood volume is only 100 to 150 c.c, we see that this loss of weight is no inconsiderable portion, especially as it was later shown that the material squeezed out was about 65 per cent. to 70 per cent. corpuscles.

Later, Barcroft was actually able to observe the changes in volume, by removing the spleen from the abdomen and sewing the inferior oblique muscle loosely beneath it, to prevent it from falling back into the abdomen. The skin and superior oblique muscle were now cut away so as to allow of placing a celluloid window in the opening. Thus all rhythmical movements in the spleen could very easily be observed. Direct analysis of the material in the splenic vein was made and the hemoglobin content of the blood was found to be 120 to 150 per cent. of the normal, so that from 1/6 to 1/4 of the total blood volume was concealed in the spleen.

Does the possession of a spleen make any difference to the organism? The answer is probably no, but in some circumstances where the hemoglobin in the spleen might be utilized, then of course the answer would be, yes. To prove this splenectomized and normal guinea pigs were placed in an atmosphere of carbon monoxide. In every case the former died first. In this case life or death depended on the hemoglobin content of the body and when an emergency arises similar to the above, then splenectomized animals are at a distinct disadvantage.

The Relation of the Spleen to Antibody Formation.

Bardach was one of the first to state that the spleen is of importance in antibody formation. In his experiments, doses of anthrax bacilli which were not fatal to normal rabbits, could kill splenectomized dogs. Tizzoni and Cattoni could not immunize splenectomized animals to tetanus, while Luckhardt showed that the spleen is the site of formation of hemolysins, hemaglutinins and hemopsonins. Moreover, rat plague caused a mortality of 89 per cent. in splenectomized animals, while it was only 28 per cent. among the normal ones. This function of the spleen is carried on by the bone-marrow and related organs after splenectomy and is due to the activities of the recticulo-endothelial system.

As regards tumour formation, we have the clinical fact that cancer metastases rarely occur in the spleen. Frankel found that injection of splenic extract was most efficient in immunizing rats against sarcomata, while more recently Parry found that the spleen offers greater resistance to injections of rat sarcomata than any other organ. Contrary results have also been obtained and the question will not be settled for some time, for tumour colonies are less easily standardized and raised in the laboratory than bacterial colonies, comparisons of virulence are difficult and vary even in the same tumours at different stages of their existence.

(As regards the other functions I shall mention them in the summary).

Summarizing, then, several facts stand out. Among other things, the spleen, though not necessary for the maintenance of life, is useful in several ways and its absence may often mean a difference between life or death. It is concerned in erythrocyte formation in foetal life and may regain this function in time of stress. It manufactures white blood cells throughout life and it may have a stimulating effect on the bone-marrow in erythrocyte formation. In the absence of the spleen it is difficult to cause hemolysis due to the decreased fragility of the corpuscles.

Barcroft's experiments have shown "that the blood volume is not a fixed part of the body-weight, but is a physiological variable which is adjusted to the work required of it and that the spleen is an integral part of the vascular system."

In regard to antibody formation most investigators hold that it plays an important role due to its recticulo endothelial system and it may also exercise some influence in the growth of tumours.

Its influence on metabolism is not so marked. That there are disturbances in digestion are supported by some and denied by others and the same applies to nitrogen, carbohydrate, fat and basal metabolism. In its relations to other organs, liver, lymph nodes, its functions are quite closely related, so that some are shared, while others are taken over after its removal.

It is thought that there is an association with the parathyroid gland following the observation that the blood calcium drops 50 per cent. after splenectomy in rabbits and in normal animals rises after injection of splenic extract. It does not seem to have any relation to the ovary and thymus gland. As regards the liver, it was mentioned above that the production of an Eck fistula causes an anemia due to the fact that the extract, if it exists, which stimulates the bone-marrow, to produce any effect, must first pass through the portal circulation to the liver.

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Classification of Mental Diseases.

BY C. B. FARRAR, M.D.

THE question of a classification is usually the first, or among the first, which the beginner in psychiatry desires to have answered. In experience it is likely to be the last to be answered, if indeed it is eventually found important to answer it at all. There can be no question that the actualities of many a mental patient have been missed through zeal for strict definition and delimitation of his "disease,"—through adherence to the view that "each disease-type is an independent self-bound entity, distinguishable from other diseases."*

The earliest classification attempts were naturally **symptomatic;** and based upon the most conspicuous aspect of the total reaction. A case of generalized excitement was **mania;** one of enduring pathological sadness was **melancholia;** one of apparent mental deterioration was **dementia.** These, however, are differentiations for which it is not necessary to invoke the aid of a psychiatrist, nor even of a physician; and they say nothing about causes, nor yet necessarily about outcomes. Symptomatic characterizations are useful just as the terms "swelling," "fever," "pain," are useful.

The starting point and hope of modern classificationists was **paresis.** Here was really a "disease" with physical symptoms, mental symptoms and demonstrable pathology. The differentiation of paresis paved the way for the recognition of other "organic" psychoses as distinguished from the "functional" group without demonstrable or presumably associated pathology of the central nervous system.

The organic-functional classification presupposed that the discovery of the histopathology of all the psychoses was only a question of extended research and refinement of technique, so that eventually psychiatry would become truly a system of mental diseases. This goal has not been attained, nor does it appear likely to be. It is hardly more to be expected that a cellular change would show the basis of a delusion or of a return of insight, than that the flash of genius which gives birth to a great poem or a haunting melody should be registered in the cortex for observation post mortem. Indeed in paresis itself, the paradigm of the organic psychoses, while the cortical changes may be regarded as the essential pathology of the disease, they do not account for the varied clinical forms the disease may assume, and they do not explain the occurrence of individual symptoms, e.g., special types of delusion. In some part at least these matters depend upon the personality traits of the patient rather than upon the specific nature of his disease.

Psychiatry was for a long time largely a descriptive science. Refinement of diagnosis depended upon increasing detail in clinical description. Disease pictures were constructed around dominant syndromes which represented elaborations of primary symptoms known and defined from time immemorial. Such was the manic-depressive psychosis of Kraepelin; which is the ever-quoted example of the functional group.

The bugbear of the earlier days of descriptive psychiatry was the uncertainty of prognosis, especially in the functional group. There were no recognized criteria by which to judge whether a "functional" case would recover or end in "secondary dementia." It was one of the major services of Kraepelin to set up in contrast the two dominant psychotic types,—manic-depressive psychosis and dementia praecox—differentiating them in symptomatology, in clinical course and in prognostic trends.

Kraepelin's conclusions had the virtue of being based upon life histories. He followed his patients through many years and looked back at the beginnings in the light of the observed facts of the end stages of disease. We are still in the Kraepelinian era and these two diseases bulk large in clinical classifications.

* Aschaffenburg: Handbuch der Psychiatrie. B. I. abt. p. 21.

But new disease pictures like social customs, enjoy a vogue and may suffer eclipse. Meynert's amentia, once frequently described, we now seldom hear of. Paranoia, the popular psychosis of the latter decades of the nineteenth century, when in certain continental institutions it included as many as three-fourths of the patient population, has now all but vanished from the text-books as an individual disease; Kraepelin in his eighth edition reckons it at less than one per cent. of admissions. Even dementia praecox ran a comparable course. At the turning of the nineteenth to the twentieth century this disease was in the ascendant and each year becoming more popular. American hospital statistics showed within a few years an increase in frequency of diagnosis of dementia praecox from nil to fifty, sixty, even eighty per cent. of admissions.

These circumstances by no means indicate corresponding changes in clinical material as the years have gone by; but they do indicate the difficulties and dangers that beset attempts at systematic classification.

However, the tendency has remained during recent years to regard a preponderating number of mental cases, barring organic conditions, those obviously a part of general intoxications, infectious or other somatic disease, the deteriorating processes of old age and the so-called psychoneuroses, as belonging either to the manic-depressive psychosis or dementia praecox.

In this situation psychiatric history continued to run true to form. It has constantly been apparent that no single description could be made elastic enough to cover all types grouped together under one diagnosis. Sub-groups have therefore been distinguished, one after another. Kraepelin describes ten varieties of dementia praecox. Another expedient has been to recognize "typical" and "atypical" forms. The atypical forms have always been uncomfortably numerous and embarrassing to the zealous classificationist. Adolf Meyer long ago observed that there were conditions which both did and did not partake of the nature of manic depressive or dementia praecox as the case might be. He suggested by way of compromise that they be designated as "allied to" these respective psychoses.

The hopelessness of making cases conform to categories is signally exemplified in the list of mental diseases officially adopted by the American Psychiatric Association, and commonly in use throughout Canada and the United States. The major groups of this classification follow:

1. Traumatic psychoses.
2. Senile psychoses.
3. Psychoses with cerebral arteriosclerosis.
4. General paralysis.
5. Psychoses with cerebral syphilis.
6. Psychoses with Huntington's chorea.
7. Psychoses with brain tumor.
8. Psychoses with other brain or nervous diseases.
9. Alcoholic psychoses.
10. Psychoses due to drugs or other exogenous toxins.
11. Psychoses with pellagra.
12. Psychoses with other somatic diseases.
13. Manic-depressive psychoses.
14. Involutional melancholia.
15. Dementia praecox.
16. Paranoia or paranoid conditions.
17. Epileptic psychoses.
18. Psychoneuroses and neuroses.
19. Psychoses with psychopathic personality.
20. Psychoses with mental deficiency.
21. Undiagnosed psychosis.
22. Conditions without psychosis.

The foregoing classification is clearly not based on any single principle and bears evidence of compromise throughout. It is valuable, however, inasmuch as its terms are generally understood, it brings some sort of uniformity into the nomenclature of psychiatry, and offers common ground upon which the various schools may meet. It is the Kraepelinian schema with modifications, although hardly improvement.

The interesting point is that under eleven of these twenty-two major headings subtypes are listed aggregating sixty-three, and that wherever such subdivisions are shown, the category "other types" is included, therefore eleven times in all. However elaborately extended the classification scheme, there must still be reserve pigeon-holes for the cases which refuse to fit.

We owe it largely to the Kraepelinian method—the study of life histories, in other words the longitudinal section of disease in contrast with the earlier symptomatic cross-section—that it inevitably drew attention not only to the spread of psychotic manifestations over the life-time of an individual, but also, and in increasing degree, to the types of personality manifesting such symptoms. The focus of attention has gradually shifted from disease to patient. We no longer deal with "cases," but with individual human beings.

It has been observed, for example, that phases of manic excitement or affect depression are not always as clear-cut as formerly supposed. Patients with this form of disability often exhibit in their normal periods traits which are suggestive of their psychotic phases, which are in fact psychotic symptoms in attenuated form. To characterize these various habitual forms of reaction we speak of constitutional affect instability; and when more definite psychotic trends are established, we recognize the hypomanic constitution, the depressive constitution or the cyclothymic constitution.

Similarly with dementia praecox. Personality traits which in their evolution lead naturally into this form of disease are commonly present, although often only retrospectively recognized, during the early developmental years of the individual affected. Moreover, praecox cases with acute phases which subside may display minor mental peculiarities which hint that recovery is not complete. Such cases have been spoken of as "recovery with defect." This viewpoint indicates that the psychotic attack has left a mental scar. While this may unfortunately be true, it is also true that the so-called defect may be no more than previously unobserved and potentially psychotic personality trends, with or without aggravation.

The foregoing facts, especially in connection with the manic-depressive psychosis which represents less pronounced departure from the normal than does the praecox reaction, indicate that the demarkation line between normal and abnormal is oftentimes very obscure, and that a given psychopathologic syndrome must be judged not only by the standard of an arbitrarily postulated norm, but also on the basis of the individual norm, i.e., the habitual reaction-mode of the person concerned.

The classification of abnormal conditions presupposes their clear differentiation from normal conditions; and this differentiation, we have learned, is not always easy to make.

Just here it is useful to refer to another group of cases, a notable characteristic of which is the vagueness of its boundaries, and which on that account is of unusual importance in psychiatric practice. These are the cases spoken of as "psychopathic personalities." They constitute a large number of the cases sometimes designated as "border types," implying a sort of half-way stage between normal and pathological. The psychopathic personality presents a permanent individual reaction mode as distinguished from the psychosis which is a morbid process contrasting in quality or degree with the habitual reaction mode of the subject. This theoretically useful distinction is, however, not always practically applicable; at least there is no agreement among authorities to that effect. Kraepelin, for example, speaks of certain psychopathic conditions as "undeveloped fore-stages of actual psychoses." Similarly Liepmanns and others make simply quantitative distinctions between psychopathic states and the well recognized psychoses.

The points of agreement as to the psychopathic personality are that it is a fixed constitutional affair and that it is less seriously pathological than the conditions we are pleased to call psychoses.

But psychoses present all degrees of severity; and taking the manic-depressive psychosis as an illustration, we have seem that there are mild and permanent constitutional types to be included under this diagnosis, and which may or may not exhibit episodic exacerbations which constitute true psychoses. But there has been not a little diagnostic half-splitting in the text-books as to which of these affect reactions should be set down as part of the psychopathic constitution and which should be classed with manic-depressive psychosis.

In keeping with the contemporary tendency to direct attention and study preferen-

tially to mild and incipient mental disorders, psychopathic personality types have come to occupy an increasingly important place in our nosologic schemes. Many types have been described and the number is really limitless. Kurt Schneider (Aschaffenburg's Handbuch) delineates ten forms, and points out that these are merely a few of the more conspicuous varieties met with.

Another pertinent consideration. Just as the normal personality alters with age, so does the psychopathic, and the change is likely to be a progressive accentuation of psychopathic characteristics. In this pathological personality evolution therefore a point may be reached where it is frankly a question of taste or habit or prejudice on the part of the observer whether he speaks of a psychopathic personality or a psychosis.

Moreover, it goes without saying that psychopathic types are in their very nature predisposed to mental upsets of various kinds. They afford perhaps the best examples of **combined psychotic reactions** which may be so disconcerting to the beginner, or to the classification idealist who feels that mental diseases should be somewhat mentally exclusive.

The contrary proves to be, if not the rule, then the conspicuous exception. A mental defective may develop a phase of excitement or depression. Mental defect and constitutional psychopathy may occur together. A manic patient may exhibit paranoid trends. A depressed case may be complicated by varied neurotic episodes. A neurasthenic reaction may initiate a grave psychosis, even paresis. Hysteroid syndromes may be succeeded by a severe schizophrenic process. Dementia praecox not infrequently develops in association with primary mental defect. The symptomatology of various organic types may be confused by psychoneurotic increments. In volutional psychoses may show, in addition to characteristic epochal symptoms, paranoidal, depressive or neurasthenic reactions. Severe forms of alcholism and drug addiction display as a rule not only toxic symptoms, bue evidences of an underlying psychopathy. Schizoid and cycloid syndromes occur in varying combinations in the same patient.

We conclude that boundary lines, whether between normal or abnormal, abnormal and pathological, or between individual psychotic trends may be difficult or impossible to define; and that psychopathology must concern itself not with diseases which have an individuality of their own and which readily lend themselves to labelling and systematic classification, nor even with syndromes per se, but rather with the ways and means by which a temporarily or permanently inadequate personality endeavors with incomplete success or total failure to adapt itself to the changing conditions of its existence. We must necessarily employ descriptive terms, and it is convenient to speak of neurotic, depressive, cycloid, paranoid, schizoid, defective, organic, senile and other reaction types. This, however, is little more than to characterize surface indications. Our inquiry must be directed to the steps in casual sequence which in the individual case and under the conditions peculiar to that case have led to the result we observe.

The traits and trends, wholesome and unwholesome, of the normal mind are multiple; the etiologic factors in every psychosis are multiple; and it need not surprise us if the symptomatic expressions of the disordered mind are likewise multiple. The only satisfactory psychiatric diagnosis is a composite one, and to be thoroughly adequate it must be individual for each patient.

The Woman Graduate in Medicine

During the last year many people have been trying to analyze the various trends in the medical profession. As an example we have the tendency for early specialization and the increasing number of full-time salaried positions. Dr. Martha Tracy, of the Women's Medical College, Pennsylvania, has compiled some statistics relating to the women graduates in medicine. It has been a question of some contention whether the activity and usefulness of the women graduates worthily repaid the extra effort essential for their education, especially in co-educational schools.

The activities of these graduates were studied in two groups, those graduating between 1905-1910 and those in the period of 1912-1921, in order to show any change in professional requirements and the effect on women physicians of the trend toward medical specialism. A total of 1,833 names were collected and questionaires sent to all. Of these 535 were returned. Since 64 were graduated in years outside of the time periods studied, 471 were left as the basis for the analyses presented.

The first facts classified related to educational qualifications. 22.5 per cent. of the 1905-1910 group held academic degrees as Bachelor of Arts before entering medical schools. In the 1912-1921 group 59 per cent. held such degrees. Hospital interneships were held by 67 per cent. in the earlier group and by 90 per cent. in the later. It is difficult to compare the percentage taking post-graduate work, since many of the later group show worthy intention, however, 40 per cent. of the 1905-1910 group and 39 per cent. of the 1912-1921 group have taken such work.

The second subject studied was that of marriage and its effect on the professional activities of the woman physician. In the earlier period 43 per cent. are married and 80 per cent. of these continued full practice —the majority being in active practice today. 93.8 per cent. of those remaining single are continuing in practice. In the 1912-21 group 44 per cent. are married, and 96.7 per cent. of those remaining single are practising. The number of women continuing full professional activity after marriage is larger than the usual assumption.

The analysis of the type of practice shows that of the women in the 1905-1910 group 58.5 per cent. are in general practice and 35.5 per cent. in special practice, whereas in the later group 39 per cent. are in general practice and 53 per cent. in special. Specialism has increased, but more in the direction of personal medical service, internal medicine, paediatrics, obstetrics and gynaecology and less in laboratory branches —this being contrary to the assumption of many casual observers. Of particular significance is the interest which tends toward the prevention of disease, not as expressed in laboratory research or sanitary engineering, but in human contacts, the personal health services in public clinics, child welfare, the call, for example, for women to organize and take charge of thoroughly adequate health maintenance services in schools and colleges. The urge toward the development of courses in individual and public hygiene for all academic students is a very real and interesting one. This interest is shown by the fact that 22.5 per cent. of the 1912-1921 group did college health work, with or without teaching together with their general practice and 30 per cent. added some public health service, such as child hygiene bureaus.

The professional incomes of women are interesting to classify. 11 per cent. of the 1905-1910 period and 17.5 per cent. of the 1912-1921 period are earning less than or up to $2,000. These are practically all in Foreign Mission Service. The largest group in both periods are earning between $2,000 and $5,000. 15.5 per cent. of the earlier group and 10.5 per cent. of the later group have incomes between $5,000 and $10,000. A few brilliant ones, 4 per cent. of the former and 2.9 per cent. of the later, earn over $10,000.

In answer to the question regarding the opportunities for the success of women in the medical profession, there was in the great majority of instances unanimity of opinion

that for the woman with good training, good personality and a willingness to work and to co-operate, there is unlimited opportunity for success. There were, however, a number of pessimists who replied that a woman must be 50 per cent. superior in the quality of her work to receive the same consideration as a medical man.

Statistics, we know, are deceiving at best and the reader should be warned against accepting these analyses as a whole, since they have been made on a small percentage of the total number of women physicians and the entire number are graduates of schools in the United States. It was not possible to contrast these figures with those of our own school. This may be done at a future date with more hopeful conclusions.

Sporting Summary, 1926-27

H. D. MARRITT, PRES. MED. ATHLETICS.

AS the year draws to a close, and one reviews the athletic activities in Medicine, it becomes quite evident that Medicine still ranks high in athletic achievements. This year's record is quite worthy of being added to the noble record set by our predecessors.

Varsity has had one of the best years in the history of the University; not only have all the cups won last year been successfully defended, but also several others have been added to the list. The undergraduates in Medicine have played a very important part in all branches of university athletics. The distribution of men on the various senior teams was as follows:

Rugby	9	men
Hockey	2	"
Basketball	5	"
Water Polo	3	"
Track	5	"
Assault-at-Arms	5	"
Soccer	3	"
Harriers	2	"
Gymnasium	2	"
Rowing	5	"

Medicine was also well represented on all intermediate and junior teams.

Between thirty-five and forty of the first "T" holders in the University are undergraduates in Medicine. This alone would indicate what an important part is taken by this faculty.

In inter-faculty athletics we finish the year with a total of three championships won, and in the play-offs in three other lines of sport. While this fell far below our ambitions, we are justly proud of the men who brought these honors to Medicine.

We started out the year right by winning the track championship. This makes two years in succession, and as the team is practically intact, we are hoping for a repeat next year. We did not fare so well in Rugby, neither the seniors or juniors reaching the play-offs. While many of our men are playing Intercollegiate Rugby, we feel that we still have enough material left to field strong Mulock Cup teams. This can only be accomplished by a keen interest being taken, and regular attendance at practice. Let's get together and bring the Mulock Cup back to Medicine next year.

The Water Polo team just about repeated again this year; they won their group, but were put out by Junior School in the two hard games in the finals. The two men on the Gymnastic Team came through with flying colours to win the championship. Junior Meds. hockey team won their group and seemed headed for the championship, but on reaching the play-offs, they were put out by the strong Dental team. Junior Meds Indoor Baseball Team was also put out in the finals. It began to look as if we were going to end the season with only two championships, especially after the first game of the finals with Victoria. However, with the never-say die spirit they came back strong, and won the second game and round by three points.

The Executive are deeply indebted to the following men for assisting in the sports mentioned:

H. Hetherington—Swimming and Water Polo.
H. Edwards—Soccer.
E. Moore—Indoor Baseball.
H. Hills—Boxing and Wrestling.

Because of the passing of the change in the Constitution, voted on at the recent elections, a card index system has been purchased with a view to keeping a record of all the athletic activities of all the undergraduates in Medicine. This record is fairly complete for the past two years, but anyone wishing to bring the record up to date previous to that time may do so by handing a record of your various activities to any member of the executive. This record is primarily to aid in the proper selection of men for receiving colours, but it should also aid managers in getting material for the verious teams, as it is intended to register up all freshmen, giving the sports taken part in previous to entering Medicine.

In graduation this year, Medicine loses the following first "T" holders:

J. L. Uren.
C. W. Potter.
K. A. Fidler.
H. D. Marritt.
E. V. Shute.
K. C. McGibbon.
J. W. R. Webster.
W. B. Snyder.

From these men the Committee chose W. B. Snyder to receive the Athletic Stick, which is given each year to a member of the graduating class, who in the opinion of the Committee, has done the most to honour his University in athletics.

The graduating class presented a very beautiful cup for competition in inter-year basketball. The cup is well named the Warren B. Snyder Cup in honour of the year's most outstanding athlete.

In inter-year activities, the following carry off the honours:

Track—2T9.
Assault—3T2.
Basketball—2T8.
Hockey—2T6.

It was hoped that all athletic awards would be presented at an open meeting, or banquet put on by the Medical Society, but as this has been impossible owing to the lack of such an event at the proper time, all awards will be distributed by the year representatives.

The following were granted the Medical Colours:

Coutts—Water Polo.
Wilford—Soccer.
Campbell—Soccer.
Ririe—Soccer.
Hollinrake—Rugby.
Railton—Rugby.
Gundy—Rugby.
Parsons—Rugby.
Inksater—Rugby.
McMillan—Rugby.
Cuddy—Rugy.
Sturgeon—Rugby.
Connor—Hockey.
Williams—Hockey.
Cock—Hockey.
Perras—Hockey.
Harris—Baseball.
Baxter—Baseball.
McTavish—Baseball.
Wright—Baseball.
A. Young—Rugby.
R. R. Goldenberg—Basketball.
S. Hurwitz—Basketball.
J. N. McEachren—Basketball.
J. H. N. Smith—Basketball.

The following in the first year will receive their "M" at the beginning of next year:

King—Soccer.
Bailie—Rugby.
Sinclair—Rugby.
Aberhart—Hockey.
Christie—Rugby.
Davey—Rugby.
Keith—Rugby.
Scott—Rugby.
J. C. Scott—Basketball.
Foex—Basketball.

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